

REMARKS

Introductory Comments

Reconsideration of the above-identified application in view of the above amendments and following arguments is respectfully requested.

Claims 17, 18, 38-41 and 43 are pending and under consideration. Claim 17 has been amended as explained below. No new matter has been added as a result of this amendment.

Applicants acknowledge with thanks the Examiner's withdrawal of the rejection under 35 U.S.C. § 102 in view of Lapidus and the rejection under 35 U.S.C. § 103 over Lapidus in view of Johansson.

Rejection of Claims 17 and 18 Under 35 U.S.C. § 102(e)

Claims 17 and 18 are rejected under 35 U.S.C. § 102(e), as being anticipated by Wittwer *et al.*, U.S. Patent No. 6,232,079 (herein "Wittwer").

Specifically, the Examiner asserts that Wittwer teaches a method for detecting a target nucleic acid sequence in a test sample as claimed (column 6, lines 1-15, column 44, lines 24-38, column 44, lines 50-67, column 45, lines 1-12, column 29, lines 13-36, column 35, lines 8-31 and column 45, lines 13-53). Essentially, the Examiner maintains the previous rejection but cites several new passages of Wittwer without explanation.

Applicants respectfully traverse this rejection.

First, the Examiner responds to Applicants' arguments on pages 8-9 of the Office Action by stating that since the claims are in a "comprising" format, any additional steps are permissible. However, Applicants previously argued that Wittwer does not disclose or teach all of the claimed steps. Briefly, Applicants argued that Wittwer does not disclose or suggest a method for detecting a target nucleic acid having step (b) of claim 17 which recites *four steps* using *four temperatures* which are all *within one cycle*. Applicants' previous arguments are incorporated herein.

While the Examiner states that Wittwer teaches dissociating the probe hybrid and activating the polymerase simultaneously, the Examiner has not addressed Applicants' arguments that Wittwer does not disclose a method comprising four steps using four temperatures in a single cycle. Furthermore, the Examiner has not cited any passages in Wittwer to refute Applicants' contentions.

While disagreeing with the Examiner's rejection, Applicants have amended claim 17 in order to expedite prosecution of the instant application. Applicants have inserted the phrase "suspected of having single or large deletions or insertions" in order to recite a method for detecting a target nucleic acid sequence suspected of having single or large deletions or insertions in a test sample". Support for this amendment can be found on page 5, lines 5-17, *inter alia*.

The method according to the present invention can be used not only to detect single base mutations, but also large deletions or insertions. In contrast, Wittwer's method is used to detect single base mutations only. See column 14, lines 32-36 and column 42, lines 62-64. Wittwer uses probes that hybridize adjacent to each other on a polynucleotide instead of using probes that hybridize on different polynucleotides. See column 5, lines 31 and 51, column 28, lines 14-16 and column 29, lines 10-15. Because of this, Applicants' method differs from that of Wittwer.

For these reasons, Applicants respectfully request withdrawal of the rejection of claims 17 and 18 under 35 U.S.C. § 102(e), as being anticipated by Wittwer *et al.*, U.S. Patent No. 6,232,079.

Rejection of Claims 38-40 and 43 Under 35 U.S.C. § 102(b)

Claims 38-40 and 43 are rejected under 35 U.S.C. § 102(b), as being anticipated by Meyer *et al.*, U.S. Patent No. 5,648,482 (herein "Meyer").

Applicants respectfully traverse this rejection.

Claim 38 recites "comparing the first signal to the second signal to determine whether a deletion or insertion of at least 50 base pairs is present in

the DNA of the test sample, wherein the amplification reagents comprise one primer that hybridizes to both the target nucleic acid sequence and the standard nucleic acid sequence" [emphasis added].

First, Applicants respectfully submit that the Examiner has misinterpreted the Meyer reference. Meyer does not disclose or suggest detecting a polynucleotide containing a deletion or insertion of at least 50 base pairs. Instead, Meyer's method is used to detect single or small base mutations. See column 10, lines 28-30, column 15, lines 38-67 and column 17, lines 16-35. The Examiner cites column 9, lines 15-40 of Meyer as teaching detection of deletions or insertions of at least 200 to 1000 base pairs. This passage states that fragments such as those containing 739 base pairs or 1123 base pairs of the CYP2D6 gene are amplified. The 739 base pairs and the 1123 base pairs are the lengths of the fragments that are amplified in order that a single or small base mutation may be detected. Meyer does not state that a deletion or insertion of 739 base pairs or 1123 base pairs is detected.

Second, Meyer does not disclose or suggest using one primer that hybridizes to both the target nucleic acid sequence and the standard nucleic acid sequence. Instead, Meyer uses two different primers because there are two separate reactions. See column 6, lines 53-59 and column 9, lines 7-65.

Therefore, Applicants respectfully request withdrawal of the rejection of claims 38-40 and 43 under 35 U.S.C. § 102(b), as being anticipated by Meyer *et al.*, U.S. Patent No. 5,648,482.

Rejection of Claim 41 Under 35 U.S.C. § 103(a)

Claim 41 is rejected under 35 U.S.C. § 103(a), as being unpatentable over the same Meyer *et al.*, U.S. Patent No. 5,648,482 in view of the same Wittwer *et al.*, U.S. Patent No. 6,232,079 as discussed above.

Specifically, the Examiner asserts that Meyer discloses all of the elements of claim 38 which claim 41 depends from, but does not disclose amplification in the presence of a probe using probe-target melting temperatures. However, the Examiner asserts that Wittwer teaches this as discussed above.

Applicants respectfully traverse this rejection.

The deficiencies of Meyer and Wittwer are stated *supra*. Applicants' arguments are incorporated herein. Applicants submit that Wittwer does not remedy the deficiencies of Meyer and vice versa.

Accordingly, Applicants respectfully request withdrawal of the rejection of claim 41 under 35 U.S.C. § 103(a), as being unpatentable over Meyer *et al.*, U.S. Patent No. 5,648,482 in view of Wittwer *et al.*, U.S. Patent No. 6,232,079.

CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. Sections 102 and 103. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Should the Examiner have any questions concerning the above, she is respectfully requested to contact the undersigned at the telephone number listed below. If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Respectfully submitted,

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